Astrocytes improve decision-making

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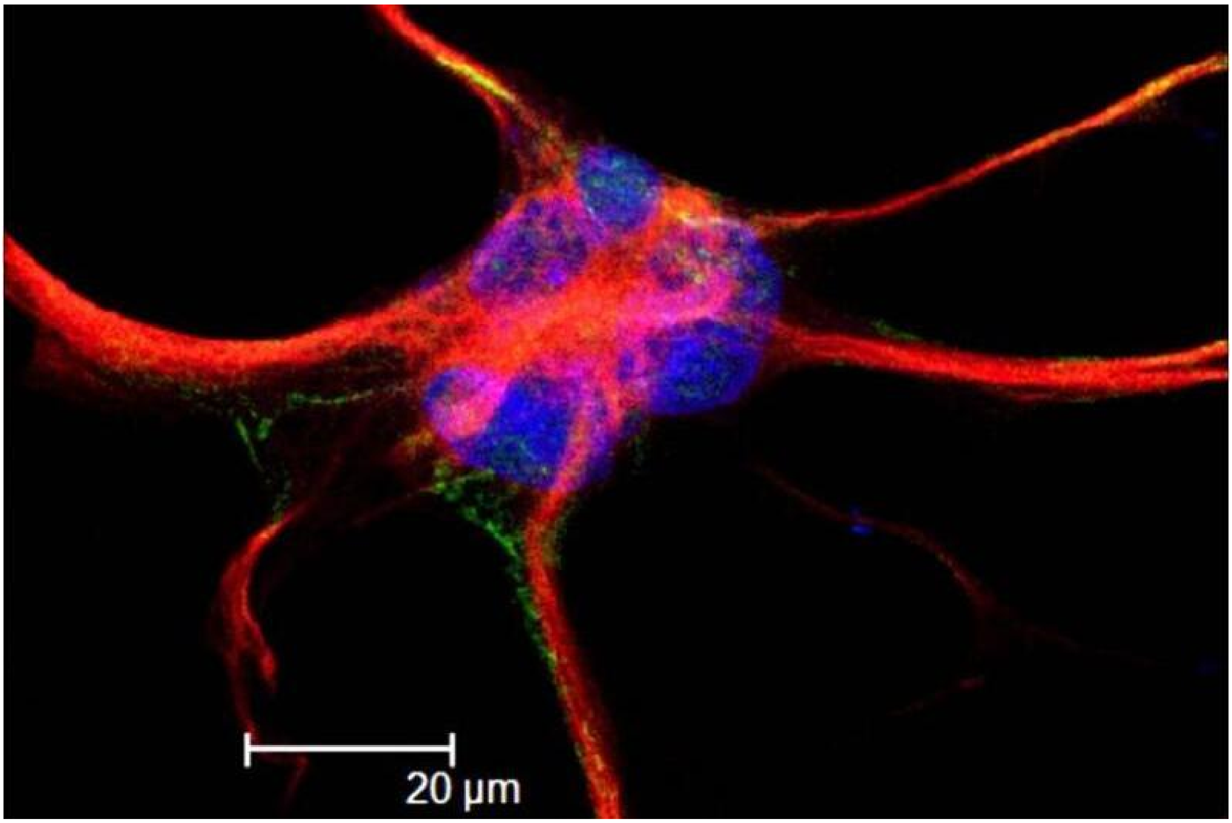

This is an astrocyte, labeled with GFAP (red), Focal Adhesion Kinase (FAK) green, and nuclear stain To-Pro (blue). Credit: Ivey and MacLean at TNPRC. Via Wikipedia.

Decision-making during goal-directed behaviors is deliberative process involving different brain areas that considers pros and cons of each option. These cognitive operations in humans and animals are crucially supported by the prefrontal cortex. In this brain region, functions of the two main classes of neural cells—excitatory pyramidal cells and inhibitory interneurons—have been extensively investigated, the sufficiency of neurons for information processing has been a long-standing assumption about brain computations. However, each brain region features also several types of glial cells, including a large population of star-shaped astrocytes.

Recent data from Dr. Perea's group suggested that, apart from the role of astrocytes in the maintenance of synaptic transmission, these cells can sense and respond to synaptically released inhibitory neurotransmitter GABA. Yet, astrocyte-neuron communication in brain circuits and its behavioral outcome remained unknown. This study aimed at investigating whether astrocytes actively participate in information processing governing behavioral actions and focused on the functional consequences of GABAergic-astrocyte signaling.

The experiments of the first author of the study Dr. Mederos in Spain and Germany and her analysis of large recorded datasets in collaboration with a leading systems neuroscience group in the U.S., showed that astrocytes in the medial prefrontal cortex modulate the balance of inhibition/excitation in neural networks controlling decision making.

Investigating the activity of multiple single neurons and local field potential in the mPFC of behaving mice, the authors found that genetic ablation of a subtype of GABA-receptors (GABABRs) in astrocytes alters the specific oscillatory gamma activity and firing properties of cortical neurons. Gamma oscillations are a form of synchronized activity of large neuronal populations. Gamma oscillations are involved in perception, working memory and other cognitive functions, and, as shown before by Dr. Ponomarenko's lab, in a dynamic engagement of the neural processing during adaptively crucial behaviors.

The activation of the prefrontal astrocytes using optogenetics, a technology for light-induced activation of cells, which have been genetically rendered light-responsive, evoked an enhancement of cortical inhibitory synaptic transmission, activation of local neurons, gamma oscillations, and improved cognitive performance. Remarkably, working memory deficits in mice with the astrocytic ablation of GABABRs could be rescued by an optogenetic stimulation of astrocytes.

This work identifies astrocytes as a hub for controlling inhibition in cortical circuits, providing an independent pathway for the behaviorally relevant midrange time-scale regulation of cortical information processing and consistent goal-directed behaviors.

The study is published in *Nature Neuroscience*.

More information: GABAergic signaling to astrocytes in the prefrontal cortex sustains goal-directed behaviors, *Nature Neuroscience* (2020). DOI: 10.1038/s41593-020-00752-x , www.nature.com/articles/s41593-020-00752-x

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